Preface to Special Topic: Selected Papers from the Advances in Microfluidics and Nanofluidics 2014 Conference in Honor of Professor Hsueh-Chia Chang's 60th Birthday

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(Received 19 October 2014; accepted 19 October 2014; published online 28 October 2014)

[http://dx.doi.org/10.1063/1.4900715]

The Fifth Conference on Advances in Microfluidics and Nanofluidics (AMN2014) was held in Academia Sinica, Taipei, Taiwan, on May 21–23, 2014. Thanks to all the invited and contributed speakers, it was a successful conference providing a highly interactive forum that brought together approximately 280 researchers in multiple disciplines from more than 21 countries and regions. This special issue is dedicated to Professor Hsueh-Chia Chang in honor of his 60th birthday and comprised the original contributions that were presented at the conference. The topics cover a wide range of research efforts from both fundamental science and practical applications of microfluidics and nanofluidics, including biosensors and diagnosis for clinical testing,[1–4] cell and evolution studies,[5–10] advanced bioimaging/optical technologies,[11,12] droplet microfluidics,[13,14] bilayer lipid membrane,[14,15] micro- and nanofabrications,[16–21] and environmental and drug screening applications.[22,23]

Integrated microfluidic devices for replacing traditional clinical tests have seen significant recent advances. Shih *et al*. designed and tested a microfluidic device for automatically carrying out enzyme-linked immunosorbent assay (ELISA) using magnetic beads on the disk platform.[1] The same group also reported an integrated microfluidic chip for testing blood coagulation using whole blood samples in 5 min.[2] The chip integrates whole blood aliquoting and metering, plasma separation, decanting, and mixing with reagents on a disk, with results from 50 clinical samples well correlated with current clinical tests. Related to this study, Chen *et al*. developed a droplet microfluidic thrombin generation assay to test inhibitors of thrombin generation, which plays a leading role in the blood coagulation cascade.[3] One challenge for microfluidic devices designed to capture target cells by affinity binding is the method of cell-release while keeping cells viable. Chang's group demonstrated a high efficiency method for releasing captured target cells in affinity-based microfluidic devices using air foam. This simple approach could be easily parallelized in a high throughput system.[4]

In the past few years, there is also significant growth of using microfluidic devices as a well-controlled environment for fundamental single cell, cell-cell interaction, or cellular evolution studies. Austin's group reported cryptic complexity in bacterial evolution using a microfluidic cell city platform with spatial stress gradients.[5] They used this device to map out the dynamics of evolution of antibiotic resistance for different *Escherichia coli* strains to address a fundamental question on evolution: Do genetically closely related organisms under identical, but strong selection pressure converge to a common resistant genotype or will they diverge to different genomic solutions? Gao *et al*. studied the regulation of cell migration and osteogenic differentiation in mesenchymal stem cells under extremely low fluidic shear stress.[6] Lee *et al*. reported measurements on how cell-to-cell interaction can affect electroporation studies of individual cells.[7] They found that cells aligned parallel to the electric field shield one another, and those oriented perpendicular to the field enhance the electroporation effect, while Luo and

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Yobas demonstrated flow-through electroporation of mammalian cells in decoupled flow streams using microcapillaries.[8] Jiang *et al*. explored how changing the geometry and chemical environment in a microfluidic channel affects the polarization of protein concentration in cells, which is a key biological process in cell division.[9] It was found that teardrop-shaped confinement induced cell polarity could be controlled with chemical cues, and the process provides new insights for understanding how cell migration may be related to cell polarity. Cheng *et al*. developed a multichannel-dual-electric-Field (MDF) chip for simultaneous chemical and electrical stimulation on lung cancer cells.[10] They found that the migration speed and the directedness toward an anode were reduced for the electrically stimulated CL1–5 cells. Suppressing Rho-associated coiled-coil kinase only eliminated the directedness of electrotropism but showed no effect on the cell migration speed. Such MDF chip will greatly shorten the experiment time and increase the accuracy of electrotaxis studies.

Advanced optical technologies can improve the observation (as witnessed by the 2014 Nobel Prize in Chemistry on super-resolution imaging) and fabrication of microfluidic devices. Patra *et al*. reported migration and vascular lumen formation of cancer cell spheroids.[11] This group combined microfluidic devices and selective plane illumination microscopy (SPIM), which gives high resolution in both spatial and temporal domain. The observation of endothelial cells in spheroids provides insight on tumor vascularization, an ideal disease model for drug screening and fundamental studies. The application of ultrafast lasers and 3D printing technology allowed the development of new methods for the production of internal microfluidic channels within the bulk of glass and polymer materials by direct internal 3D laser writing. O'Neill *et al*. reviewed the latest advances in the production of microfluidic 3D structures,[12] in which current applications of these rapid prototyped microfluidic platforms in biology were discussed.

Lee *et al*. developed a novel, multi-scale approach that combined molecular dynamics (MD) and lattice Boltzmann (LB) modeling methods to study the rheological properties of a droplet emulsion.[13] The droplet surface tension is modeled with near atomistic details using MD. The interfacial tension is then used as an input parameter to LB which captures shear-thinning of the droplet emulsion. Multi-scale modeling efforts such as this study could pave the way of understanding how molecular interactions could have large-scale consequences on the dynamics of the bulk suspension. Fan *et al*. experimentally studied the formation of suspended bilayer lipid membrane between electrowetting-driven encapsulated droplets.[14] They used limited lipid molecules held by two water-core/oil-shell encapsulated droplets and formed an optically observable bilayer lipid membrane across a microfabricated aperture. This study shows the influence of the lipid concentration to the interfacial tension and electrowetting-on-dielectric. While in another study, Chao's group adopted an innovative phase segregation scheme of polymerizable lipids in supported lipid bilayer platforms to construct filters for separating lipid-membrane-embedded species such as Texas-Red DHPE (1,2-dihexa-decanoyl-snglycero-3-phosphoethanolamine triethylammonium salt) and cholera toxin subunit B-GM1 complex.[15]

Further, advanced micro/nanofluidic fabrication schemes and applications and sample analysis were demonstrated. Ouyang and Wang used triple thermal oxidation and silicon-glass anodic bonding for the fabrication of sub-100/10 nm planar nanofluidic channels.[16] Moon *et al*. proposed a unique strategy of microfluidic conformal coating of non-spherical magnetic particles in a co-laminar flow microfluidic system.[17] Sheng *et al*. deployed atomic layer deposition to modify polymer nanopores for the fabrication of nanofluidic diodes.[18] Rohani *et al*. revealed a method of quantifying spatio-temporal dynamics of biomarker pre-concentration and depletion in microfluidic systems by intensity threshold analysis.[19] Chou's group developed a new DNA combing platform using low-pressure oxygen plasma modified polysilsesquioxane substrates for single-molecule studies and used it to observe DNA-protein complexes and the effect of cancer drug cisplatin on DNA conformation.[20] With the aid of a simulation study, Yoon *et al*. proposed a new way of measuring fluid interfacial nanoroughness through the morphological characteristics of graphene.[21]

Microfluidic devices could also play important roles for environmental and drug screening applications. Liu *et al*. reported a portable lab-on-a-chip system for detecting metal ions in water using gold nanoparticles.[22] They designed a microwell plate with a handheld colorimetric reader and demonstrated that this portable system provided limits of detection of 30 ppb for

detection of Pb2+ and 89 ppb for Al3+, both comparable to bench-top analytical spectrometers. Zhao and Chen adopted transverse diffusion mediated capillary microanalysis for the effective screening of neuraminidase inhibitors from traditional Chinese medicine.[23]

We would like to express our special thanks for the financial support from the Ministry of Science and Technology (Taiwan), American Institute of Physics, the Vice President Office, Institute of Physics, and Research Center for Applied Sciences of Academia Sinica, National Center for Theoretical Sciences, and the exhibitors, and to the conference secretariat led by Shin-Chuen Hsieh, in making AMN2014 a successful and wonderful addition to the AMN conference series. Our thanks also go to Leslie Yeo, Jennifer Simmerer, and all the staff from Biomicrofluidics for their kind assistance during the preparation and, most importantly, to all the authors who have contributed their work for this special issue.

[1]C.-H. Shih, H.-C. Wu, C.-Y. Chang, W.-H. Huang, and Y.-F. Yang, Biomicrofluidics **8**, 052110 (2014).
[2]C.-H. Lin, C.-Y. Liu, C.-H. Shih, and C.-H. Lu, Biomicrofluidics **8**, 052105 (2014).
[3]J. Yu, D. Tao, E. X. Ng, C. L. Drum, A. Q. Liu, and C.-H. Chen, Biomicrofluidics **8**, 052108 (2014).
[4]J.-M. Lai, H.-J. Shao, J.-C. Wu, S.-H. Lu, and Y.-C. Chang, Biomicrofluidics **8**, 052001 (2014).
[5]Q. Zhang, J. Bos, G. Tarnopolskiy, J. C. Sturm, H. Kim, N. Pourmand, and R. H. Austin, Biomicrofluidics **8**, 052004 (2014).
[6]X. Gao, X. Zhang, H. Xu, B. Zhou, W. Wen, and J. Qin, Biomicrofluidics **8**, 052008 (2014).
[7]B. E. Henslee, A. Morss, X. Hu, G. P. Lafyatis, and L. J. Lee, Biomicrofluidics **8**, 052002 (2014).
[8]Y. Luo and L. Yobas, Biomicrofluidics **8**, 052101 (2014).
[9]W. Zheng, Y. Xie, K. Sun, D. Wang, Y. Zhang, C. Wang, Y. Chen, and X. Jiang, Biomicrofluidics **8**, 052010 (2014).
[10]H.-S. Hou, H.-F. Tsai, H.-T. Chiu, and J.-Y. Cheng, Biomicrofluidics **8**, 052007 (2014).
[11]B. Patra, Y.-S. Peng, C.-C. Peng, W.-H. Liao, Y.-A. Chen, K.-H. Lin, Y.-C. Tung, and C.-H. Lee, Biomicrofluidics **8**, 052109 (2014).
[12]P. F. O'Neill, A. Ben Azouz, M. Vázquez, J. Liu, S. Marczak, Z. Slouka, H. C. Chang, D. Diamond, and D. Brabazon, Biomicrofluidics **8**, 052112 (2014).
[13]S. B. Choi, H. M. Yoon, and J. S. Lee, Biomicrofluidics **8**, 052104 (2014).
[14]S.-K. Fan, C.-W. Chen, Y.-Y. Lin, L.-C. Chen, F.-G. Tseng, and R.-L. Pan, Biomicrofluidics **8**, 052006 (2014).
[15]S.-K. Hu, Y.-M. Chen, and L. Chao, Biomicrofluidics **8**, 052005 (2014).
[16]W. Ouyang and W. Wang, Biomicrofluidics **8**, 052106 (2014).
[17]B.-U. Moon, N. Hakimi, D. K. Hwang, and S. S. H. Tsai, Biomicrofluidics **8**, 052103 (2014).
[18]Q. Sheng, L. Wang, C. Wang, X. Wang, and J. Xue, Biomicrofluidics **8**, 052111 (2014).
[19]A. Rohani, W. Varhue, Y.-H. Su, and N. S. Swami, Biomicrofluidics **8**, 052009 (2014).
[20]K. K. Sriram, C.-L. Chang, U. Rajesh Kumar, and C.-F. Chou, Biomicrofluidics **8**, 052102 (2014).
[21]H. M. Yoon, J. S. Lee, J.-S. Yeo, and J. S. Lee, Biomicrofluidics **8**, 052113 (2014).
[22]C. Zhao, G. Zhong, D.-E. Kim, J. Liu, and X. Liu, Biomicrofluidics **8**, 052107 (2014).
[23]H. Zhao and Z. Chen, Biomicrofluidics **8**, 052003 (2014).